## REMARKS

Claim 1 and claims 4-6 dependent thereon and claim 14 have been amended to read only on nucleic acids which comprise a nucleotide sequence encoding an $\alpha_{1G}$ subunit that has an amino acid sequence at least 99% homologous to SEQ ID NO: 24 or that has a sequence that is identical to that of SEQ ID NO: 37. The $\alpha_{1G}$ subunit-encoding nucleic acid sequence set forth as SEQ ID NO: 5 in U.S. patent 6,358,706 no longer falls within the scope of the amended claims. Claim 2 and new claim 19 claim nucleic acids comprising nucleotide sequences that encode SEQ ID NO: 24 or SEQ ID NO: 37 claimed individually. Similarly, such parsing of individually claimed sequences is reflected in the amended claim 18 and new claim 26. New claims 20-25 are revised forms of claims 4, 5 and 6 which reflect the limitations of claim 2 and claim 19; they differ from the subject matter of claims 4-6 only in their dependency.

Claim 6 has been amended to insert the word "recombinant" and applicants appreciate the helpful observations and suggestions made by the Examiner in this regard. No new matter has been added and entry of the amendment is respectfully requested.

The Rejection Under 35 U.S.C. § 112, Second Paragraph

Only claim 6 was the subject of this rejection, and it has been amended as suggested by the Examiner. Again, applicants appreciate the suggestion and are happy to adopt the solution to the problem identified.

The Rejection Under 35 U.S.C. §§ 101 and 112, First Paragraph

All examined claims were rejected as lacking utility and thus not complying with 35 U.S.C. §§ 101/112. Before responding in detail to the points raised by the Office applicants wish

to clarify what they consider to be the utility of the recombinant materials and methods claimed. Briefly, these materials and methods are useful to produce $\alpha_{1G}$ calcium ion channel subunits which are used in screening assays to identify compounds that can be employed to treat conditions that are the result of inappropriate T-type calcium ion channel activity. As stated on page 12, beginning at line 29:

> The resulting cell lines expressing functional calcium channels including the $\alpha_1$ subunits of the invention can be used to test compounds for pharmacological activity with respect to these calcium channels. Thus, cell lines are useful for screening compounds for pharmaceutical utility.

The nature of the pharmaceutical utility is spelled out in the specification, for example, on page 5 at line 14:

> The resulting identified compounds are useful in treating conditions where undesirable T-type calcium channel activity is present. These conditions include epilepsy, sleep disorders, mood disorders, cardiac hypertrophy and arrhythmia and hypertension among others.

Thus, the utility of the recombinant materials is spelled out in the specification in the context of ultimately identifying compounds useful in treating specific conditions set forth in the specification.

While it is certainly the case that such compounds have not yet been identified, the utility of providing screening tools to identify such compounds has long been recognized. There is a multiplicity of patents issued based on this proposition. For example, U.S. 6,358,706, cited by the Office, which discloses an $\alpha_{1G}$ subunit with a somewhat different sequence, issued with claims similar to those proposed herein. The utility as recited in this patent is precisely that claimed here. Column 16 of '706, beginning at line 42, recites that assays are provided to identify compounds that modulate the $\alpha_{1G}$ subunit associated channels; at column 17, beginning at line 17, the conditions

which can be treated with such modulators are identified. These conditions include a fairly long list; the conditions identified herein are in fact on this list.

Similarly, in *Bayer AG v. Housey Pharms., Inc.*, 340 F3d 1367, 68 USPQ2d 1001 (Fed. Cir. 2003) claims to "a method of determining whether a substance is an inhibitor or activator of a protein whose production by a cell evokes a responsive change in phenotypic characteristics" were asserted. The defendant had apparently imported information as to the results of this assay into the U.S. in order to identify useful drugs. The case then turned on the fact that 35 U.S.C. § 271(g) (which finds infringement upon importation of the product of a patented process) was not applicable to a screening test. There was no issue as to the utility of this claim.

Similarly, in *Sibia Neurosciences, Inc. v. Cadus Pharmaceutical Corp.*, 225 F3d 1349, 55 USPQ2d 1927 (Fed. Cir. 2000) the asserted claims were directed to a method for identifying compounds that modulate cell surface protein mediated activity. The claims were invalidated as obvious, not because they lacked utility.

Finally, in the *University of Rochester v. G. D. Searle & Co.*, 358 F3d 916, 69 USPQ2d 1886 (Fed. Cir. 2004) the Court took note of claims that were not challenged covering methods "for identifying a compound that inhibits prostaglandin synthesis catalyzed by mammalian prostaglandin H synthase-2" in U.S. patent 5,837,479. The Court found invalidity only of claims directed to methods for selectively inhibiting PGHS-2 activity in a human host by administering a non-steroidal compound that did this, where the compound was not identified.

In short, there appears to be no question of the utility with respect to claims directed to methods and materials to screen for compounds where the utility of the compounds that are successful in the screen is understood.

A review of the examples in the Utility Guidelines (issued in 1999) seems to give only one relevant example, where claims are based on a "receptor." Lack of utility was found only because there was no disclosure in the art or the specification of any diseases or conditions associated with the receptor. That is not the case here where both the specification and the art disclose such conditions.

There are dozens of patents issued directed to methods to screen or identify compounds that would be useful in treating particular indications; provided the condition that the successful compound will be useful in treating is identified, there appears to be no question that such methods are useful, and therefore the materials required for these methods are useful as well.

Turning to the specific points raised by the Office, applicants do not agree that utilities related to designing peptides to produce antibodies to assess location and expression of the protein or to producing proteins in cell lines to determine the properties of the channels are insufficient. However, these are not relied upon by applicants. The utility on which applicants rely is that discussed on page 4 of the Office action in the paragraph enumerated as "3", which is the use of cell lines to evaluate the effects of pharmaceuticals or toxic substance on calcium channels that incorporate the subunits of the invention.

Applicants appreciate the acknowledgement that this utility is credible, but assert that it is specific and substantial. While it is true that any recombinantly expressed protein could be used in an assay to determine the effects of unnamed compounds on itself, the particular assay here is specific in that the effects of the compounds are assessed with respect to their ultimate ability to treat the conditions associated with inappropriate activity of the calcium ion channel. Thus, the assay is specific to these conditions and is substantial in that it promises a useful pharmaceutical

outcome. The Office states that the evaluation of pharmaceuticals and/or toxins on channels is basic research as discussed in Hille, pages 59-62. Applicants are not certain why, exactly, this point is made, perhaps it will suffice to point out that while this can be the purpose, it need not be, and is not the purpose in terms of the utility of the present invention. Here, rather than analyzing the mechanism of action, etc., of the channel, the point is to find specific compounds that will be useful in the treatment of specific conditions.

In the next statement, the Office asserts that applicants have not disclosed a specific nexus between a disease and the polypeptide encoded by the polynucleotides of the invention. This is not the case. As noted above, these conditions are set forth in detail on page 5 of the specification at lines 14-17 as well as page 9, lines 19-23. Thus, the analogy to the DNA diagnostic where the condition being diagnosed is not known is inappropriate here, where the condition to be treated is known.

The Office goes on to state that T-type channels are heterogeneous and therefore conditions associated with other T-type calcium channels known in the art may not be associated with the T-type calcium channel of the present invention. There are two problems with this. First, applicants need not rely on the art because the conditions that form a nexus with the T-type channel whose recombinant materials are being claimed are set forth in the specification. Second, the heterogeneity to which the cited Yunker document refers is that of $\alpha_{1G}$, $\alpha_{1H}$ and $\alpha_{1I}$. As noted above, U.S. 6,658,706 is directed to recombinant materials for the production of $\alpha_{1G}$ subunits, as are the claims in the present application. Therefore, in addition to the conditions set forth in the specification as associated with this type of calcium ion channel, those set forth in '706 may also be taken into account.

Applicants recognize that the facts in *In re Brana*, *Burroughs-Wellcome v. Barr*, and *In re Cortright*, are not on all fours with the present case. The significance of *In re Brana* is simply that ultimate clinical utility of a compound which is identified in a model need not be established. This is equally applicable to the present situation where the model is the subject of the claim as opposed to the compound thus identified.

Respectfully, in terms of real world usage, screens based on recombinantly produced receptors or ion channels whose nexus to a disease or condition is known are used every day in the pharmaceutical industry and there is a plethora of patents directed to recombinant materials whose utility is precisely their use in such screens. Accordingly, applicants believe that this basis for rejection may properly be withdrawn.

The Rejection Under 35 U.S.C. § 112, First Paragraph, Written Description

Applicants do not understand the rejection starting on page 8 made under this paragraph. At the bottom of the page, the Office states "however, the claims are (sic, as?) currently written include nucleic acid sequences that may encode functional $\alpha_{1G}$ subunits." It is unclear why this leads to a rejection based on lack of written description, and it is unclear why the proposed recitation of functional limitations would be helpful. As explained in the specification, $\alpha_1$ subunits of T-type receptors are in many instances able to facilitate the transport of calcium ion when expressed alone; however, this can be modulated by association with other subunits. (See page 4, line 15.) Thus, functional $\alpha_{1G}$ channels would include the function of transporting calcium ions when expressed alone as well as in association with other subunits.

It is unclear what type of written description is lacking. As the Office is aware, the written description requirement is separate from enablement in requiring that the applicants demonstrate

possession of the invention, *Vas-Cath Inc. v. Mahurkar*, 935 F2d 1555, 19 USPQ2d 1111 (Fed. Cir. 1991). The phrase "wherein the polypeptide transports calcium" does not seem to indicate one way or the other whether applicants are in possession of the invention.

Priority

Applicants believe that claims as they relate to SEQ ID NO: 24 are entitled to the benefit of parent application Serial No. 09/346794 and that claims as they relate to SEQ ID NO: 37 are entitled to the filing date of the present application. As argued extensively above, the utility and enablement requirements are met both in the present application and, for similar reasons, in the parent.

The Rejection Under 35 U.S.C. § 102

The claims have been amended to obviate the incidental anticipation of sequences homologous to SEQ ID NO: 37 and thus obviate this basis for rejection. Applicants note with appreciation that claims 2 and 18 which are directed to nucleic acids with nucleotide sequence encoding SEQ ID NO: 37 or SEQ ID NO: 24 *per se* are not included in this rejection. Based on the amendment, this basis for rejection may be withdrawn.

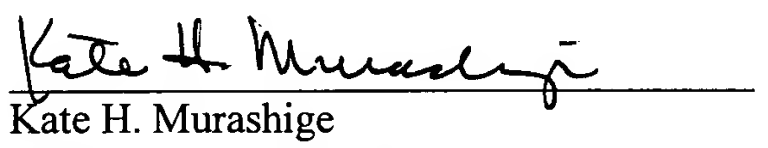
Conclusion

The utility of the recombinant materials and methods is to provide the required tools to conduct methods to identify compounds that would be employed in treating specified conditions such as epilepsy, hypertension, and the like as set forth in the specification. The utility of methods to identify compounds useful in treating specified conditions is well recognized. The claims have been amended to avoid accidental anticipation by a sequence set forth in the art. It is believed that

all substantive rejections are overcome and passage of the examined claims, claims 1-2, 4-6, 14 and 18-26 to issue is respectfully requested.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicants petition for any required relief including extensions of time and authorize the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket No. 381092000721.

Respectfully submitted,

Dated: March 22, 2005 By: 

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